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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/090,965	SRIENC ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/10/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on January 10, 2005, canceling claim 94, has been entered.

Claims 1-13 are pending and are under consideration.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on January 10, 2005 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Response to Arguments

Applicant's arguments filed on January 10, 2005 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Madison et al., Clemente et al. and Lee et al.

Claims 1-13 are drawn to a method of producing PHA in *S. cerevisiae* or *Kluyveromyces by* introducing polynucleotide encoding a PHA_{SCL} or PHA_{MCL} and a polynucleotide encoding an acetoacetyl-CoA reductase and/or a β-ketothiolase.

Madison et al. teach a method of producing PHA in *S. cerevisiae* by introducing DNA encoding an *A. eutrophus* PHA polymerase (page 44). Madison et al. teach that low levels of PHA was due to insufficient activity of the endogenous β-ketothiolase and acetoacetyl-CoA reductase and points to improving PHA yields in *S. cerevisiae* by increasing the activities of these two enzymes.

Further, Madison et al. teach other PHA_{SCL} and PHA_{MCL} that can be used in transgenic yeasts (pages 24-35) and that many different transgenic organisms can be used to produce PHA (page 44), such as a Kluyveromyces, which also belongs to the family of Saccharomycetaceae like *S. cerevisiae*.

The difference between the reference of Madison et al. and the instant invention is that the reference of Madison et al. does not teach a method of producing PHA using a transgenic yeast comprising transforming the yeast cell with polynucleotides expressing either β-ketothiolase or acetoacetyl CoA reductase in addition to PHA_{SCL} or PHA_{MCL} or to express three heterologous in a single nucleic acid construct such that it results in increase production of PHA.

However, expression of multiple heterologous genes in yeast is routine in the art. Also, making a single nucleic acid construct composed of more than one or two genes

is also very routine in the art (Strategene catalog, cited in previous Office Action). For example, Clemente et al. (U.S. Patent No. 5,489,894 – form PTO-892) teaches a method of expressing three genes via a single nucleic acid construct (Columns 15-16).

Also, production of polyhydroxyalkanoates using anaerobic/fermentation methods are well known and performed in the art. For example, Lee et al. (form PTO-892) teaches a method of producing polyhydroxyalkanoates using fermentative methods to increase efficiency in producing polyhydroxyalkanoates (abstract). Clemente et al. also uses fermentative/anaerobic conditions in producing polyhydroxyalkanoates (Columns 4-5, Example I). Although Lee et al. uses bacteria, one of ordinary skill in the art can apply similar methodology in producing polyhydroxyalkanoates using yeast in anaerobic conditions.

Therefore, with the teaching of Madison et al. in hand it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a transgenic *S. cerevisiae or Kluyveromyces* yeast comprising the heterologous PHA polymerase, β-ketothiolase and/or acetoacetyl CoA- reductase. The motivation of further expressing said enzymes via a single nucleic acid construct is to control and increase activity of said enzymes to increase the yield of PHA. The motivation of producing polyhydroxyalkanoates under fermentative/anaerobic conditions would be to increase efficiency of the production of polyhydroxyalkanoates. One of ordinary skill in the art would have had a reasonable expectation of success since Madison et al. teach that an increase in activity of β -ketothiolase and an acetoacetyl CoA- reductase in yeast transformed with PHA_{SCL} or PHA_{MCL} will increase the yield of PHA and Lee et al.

teaches that production of polyhydroxyalkanoates can be increased by using fermentative/anaerobic conditions.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that claim 1 does not stipulate three nucleic acid fragments nor that that they must be present on a single nucleic acid construct and that the Examiner has inadvertently mischaracterized the invention. In order to address that argument, Examiner has re-written the rejection. Furthermore, claims are give their broadest reasonable interpretation, see MPEP 2111.

Applicants argue that the teachings of Clemente et al. is limited to bacteria and plants and mention of yeast as a host organism is absent. While Clement et al. disclose using bacteria, the reference of Clement et al. is relied upon only to demonstrate that constructing a single polynucleotide comprising several genes was known in the art. A page from *Strategene* was cited to demonstrate expression of more than one gene in yeasts. Therefore, one having ordinary skill in the art would have had a reasonable expectation of expressing a single polynucleotide sequence comprising several genes in yeast. Expression of a single polynucleotide sequence comprising several genes is not a unique feature only in bacteria.

Applicants argue that Madison et al. is silent on the culture conditions (aerobic vs. anaerobic) but applicants also state that Madison et al. reports aerobic conditions. Therefore, Madison et al. is not silent on the culture conditions.

Applicants argue that "fermentation" does not necessarily imply "anaerobic culture conditions" and therefore there is no motivation or suggestion to use anaerobic culture conditions in producing PHAs. Examiner respectfully disagrees. Fermentation is an enzymatically controlled anaerobic breakdown of an energy-rich compound. Upon the teachings of Lee et al. and Clemente et al., one having ordinary skill in the art would have recognized to produce PHA under anaerobic conditions in order to increase the yield of PHAs.

Applicants argue that transgenic bacterial cells were restricted from transgenic yeast cells and therefore, they are patentable over each other. Examiner respectfully disagrees. Since Madison et al. discloses a method of producing PHAs using transgenic yeasts and not transgenic bacteria, the relevance of applicants' arguments is not clear.

None of the claims are allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652

Manjunath Rao
Primary Examiner 1652